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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,549	SCHNABELRAUCH ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-39* is/are pending in the application.

4a) Of the above claim(s) *32-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 9-31* is/are rejected.

7)☒ Claim(s) *2,26 and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *26 May 2006 and 3 April 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO REMARKS

The Examiner thanks the Applicants for their timely reply filed on 19 November 2009, in the matter of 10/580,549. The Examiner acknowledges the following:

Claim 8 has been cancelled and amended into claim 1.

No additional claims have been added, amended or cancelled.

Thus, no new matter has been added.

Applicants' remarks regarding the amended pending claims 1-7 and 9-39 have been fully considered, but are unpersuasive.

Applicants' election **with traverse** of Group I (claims 1-7 and 9-31) is acknowledged. Applicants traverse the restriction requirement alleging that since "no lack of unity objection [was] made in the corresponding international application as noted in the International Preliminary Examination Report … the restriction is improper."

In response, the Examiner respectfully submits that Applicants' have provided no supportive grounds for reconsidering the lack of unity restriction set forth.

Per PCT Rule 13.1, the international application shall relate to a group of inventions so linked as to form a single general inventive concept or a "unity of invention" (see MPEP 1850). Per PCT Rule 13.2, said "unity of invention" is fulfilled by defining a special technical feature that is shared amidst the claimed inventions. The Rule further specifies that "[t]he expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, **makes over the prior art**." The recitation of generic subject matter in the base claims is sufficient enough to demonstrate a lack

of unity amidst the groups set forth in the previous Office Action. This is clearly evidenced by the teachings of Deibig over the instantly claimed composition (see previous Office Action, pg. 3, first full paragraph).

Applicants' election **with traverse** of the constituent species: of "water-soluble pore-forming substance" in claim 8 (now in claim 1) is further acknowledged and has also been fully considered.

Despite Applicants' unpersuasive remarks traversing the election of species, the Examiner has fully reconsidered the Election of Species previously set forth, in light of the state of the art, and **withdraws** said requirement.

The restriction requirement is hereby made **FINAL**. The remaining claims 32-39 (Groups II-IV) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Applicants timely traversed the restriction requirement between the compositions and method claims.

Thus, claims 1-7 and 9-31 are presented and represent all claims under consideration.

INFORMATION DISCLOSURE STATEMENT

Two Information Disclosure Statements (IDS), filed 26 May 2006 and 3 April 2007, are acknowledged and have been considered.

SPECIFICATION

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a

basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) **if a process, the steps**.

Extensive mechanical and design details of apparatus should not be given.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

ARRANGEMENT OF THE SPECIFICATION

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.

(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

CLAIM OBJECTIONS

Claims 2, 26 and 30 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants are required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form.

Concerning claim 2, "constituents which modify the properties of the monomer, monomer mixture and/or composite material" are already mixed in, per Applicants' amendment to claim 1. As such, claim 2 is considered and interpreted as not further limiting the base claim as well as reciting the same subject matter.

Claim 26 depends directly from claim 25, which depends directly from the base claim. Claim 25 recites that the bone regeneration material recited in step (i) (BRM_i) is the same as that which is used in step (ii) (BRM_{ii}). Claim 26 then recites that BRM_i and BRM_{ii} are different. The claim is interpreted to be not further limiting since it is unclear how the bone regeneration material may first be the same and then be different.

Claim 30, broadly and reasonably interpreted, recites a limitation to claim 2, objected to above, wherein constituents are added which are both biocompatible and which modify the

properties of the regeneration material. Given that this limitation appears to be recited in both claims 1 and 2, claim 30 is not considered to further limit the invention, as presently recited.

CLAIM REJECTIONS - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim a method for producing a self-hardening, bioabsorbable composite material (e.g. a bone cement) which further comprises a pharmaceutically active ingredient or mixture thereof for prophylaxis (claims 1 and 13). Claim 14 recites such general categories of drugs as proteinogenic growth factors and cancerostatics as being the agents which accomplish the prevention. A method of remediation is also interpreted by the Examiner as being claimed in so much as the active(s) which may be included contribute to some form of "prophylaxis" when the composite which is made, is administered.

The test of enablement is whether one of ordinary skill in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Teletronics, Inc.,* 8 USPQ2d 1217 (Fed. Cir.

1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors are outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) and include the following:

UNPREDICTABILITY IN THE ART. The promotion of health and treatment or prevention of diseases using antibiotics, anti-inflammatories, "proteinogenic growth factors" and "cancerostatics" is complex and unpredictable. This unpredictability is derived, first, from the common knowledge in the art that antibiotics and anti-inflammatories are known for treating and fighting infection (see for Example Draenert et al., discussed herein). Unpredictability is further derived from Applicants' lack of description which fails to provide any description of that which is intended treated prophylactically as well as a description of the specific compounds which would accomplish such a treatment. The vast majority of the prior art concerning antibiotics, anti-inflammatories and cancer-treating active agents (e.g. antiproliferatives) teach their use as treatments for reducing the presence, occurrence, or likelihood of ailments such as cancer and/or inflammation. Remedies that prevent, as opposed to treat, are rarely, if ever taught in the prior art. The prior art discussed herein under the 103(a) rejection below, different teachings on the use of the individual antibiotic components of the instant composition which serve to lessen the likelihood for incurring an inflammatory response.

NATURE OF THE INVENTION. The invention involves incorporating one or more pharmaceutically active ingredients into a self-hardening bone composite material which is

ultimately administered "for local and/or prophylaxis" (per claim 13). Therefore, the invention is considered experimental.

STATE OF THE PRIOR ART. The art does not recognize prophylaxis (e.g. prevention) using the very generally claimed and described ingredients, individually or in concert.

NUMBER OF WORKING EXAMPLES. Applicants present no working examples which incorporate any pharmaceutically active agent recited or discussed in the instant disclosure. As such, not one of the examples provided demonstrates the ability for the invention to treat or prevent anything.

BREADTH OF THE CLAIMS. The scope of the invention is considered to be extremely broad given the aforementioned lack description surrounding pharmaceutically active ingredients which elicit preventative or prophylactic properties in a bone cement. The broadest claim reads on the preparation of a self-hardening bone composite material.

AMOUNT OF GUIDANCE PROVIDED. Applicants provide no specific guidance for useful treatment, prophylaxis or prevention of cancer and/or inflammation. Applicants only provide generic teachings indicating that the instantly recited pharmaceutically active bone composites can be used as a means for treating or preventing unspecified conditions. Applicants disclose on page 15, lines 6-12, that "pharmaceutically active ingredients [or their mixtures], released from the composite material after implantation may be used for local therapeutic or prophylactic treatment of the tissue located within the vicinity of the composite material."

Merriam-Webster Online Dictionary defines the term "prophylaxis" as measures designed to preserve health and prevent the spread of disease, and the term "prevent" as keeping from happening or existing. Thus, given the overlap of the definitions of the terms and in employing their broadest, most reasonable interpretations, the Examiner maintains that Applicants' claim to the prophylactic treatment in a subject are not supported and that no teachings are presented as to how the skilled artisan would use the instantly recited bone composite for treatment, prevention, or prophylaxis of *any* condition.

LEVEL OF SKILL IN THE ART. The level of skill in the arts of therapeutic bone composite formulation, administration, treatment and/or prevention is high. However, given the unpredictability of the art, the poorly developed state of the art with regard to the use of instant composite formulation for treatment and prevention of unspecified conditions and the lack of guidance in the practice of the invention, said skilled artisan would need to have conducted essentially trial and error experimentation in order to practice the claimed invention.

Given the analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have needed to have conducted an undue and excessive amount of experimentation in order to practice the claimed invention.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter that is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventors, at the time the application was filed, had possession of the claimed invention. Claim 14, as discussed above, recites such general pharmaceutically active ingredients as "proteinogenic growth factors". While the Examiner acknowledges that the term "proteinogenic growth factors" is mentioned in the instant specification, the term is not defined by the instant specification in a clear and concise manner. As such, the disclosure of the instant specification is not sufficient to support the generic concept of "proteinogenic growth factors" and requires further clarification. A brief search of the prior art concerning the instantly claimed term resulted in the instant application only. At present, it appears that no clear definition may be construed from the prior art, and the Examiner is unable to interpret the term for the purposes of examination on the merits.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 5, 10-11, 14, 19, 24, 26 and 27-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim

indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, each of the aforementioned claims 2, 5, 10-11, 19, 24 and 27-31 present broad recitations, which are then followed by narrower statements of the ranges or limitations which are "preferably" and/or "especially" claimed.

The recitation of the term "cancerostatic" as a pharmaceutically active ingredient renders the instant invention indefinite particularly since it is unclear whether Applicants intend this type of agent as being one which is treats cancer (e.g. remission) or prevents cancer. Given the broadest reasonable interpretation of the term, absent a clear definition provided by Applicants, the Examiner interprets the limitation as reciting such general compound types as "antiproliferative" compounds (e.g. paclitaxel).

Claim 26, as recited renders the instant invention indefinite. Claim 1 recites that the two amounts of bone regeneration material used in steps (i) and (ii) may either be the same or different. Claim 25, which depends directly from claim 1, further limits this option to where they are the same. Claim 26 then recites that they are different. Since claim 26 depends directly from claim 25, it is unclear how the invention may be directed to both options simultaneously. Clarification is respectfully required.

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 9-11, 15, 18-19, 21-26 and 28-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Schnabelrauch et al. (Machine translation of German Patent DE 199 39 403 A1; the original submitted by Applicants).

The instant invention of claim 1 is drawn to a method for producing a self-hardening bioabsorbable composite, wherein a polymerization initiator ("initiator") is mixed with an interconnectingly porous bioabsorbable inorganic bone regeneration material (herein, "bone regeneration material" or "BRM") and a polymerization activator (herein "activator") is also mixed with a bone regeneration material. The bone regeneration material in the case of the separate mixings may either be the same or different. The initiator mix and activator mix are then combined with one another with a third component which is a multi-functional monomer(s), which is in either liquid or paste form. An additional limitation to the base claim is that at least one of the constituents mixed therein is a water-soluble pore-forming substance which is added to the monomer(s). Claims 3 and 4 recite that one or more modifying constituents are added to the mixture (e.g. thickeners or viscosity modifier). Claims 5 and 6 further limit claim 4 in terms of the composition of the viscosity-modifying constituent (e.g. dianhydro-D-glucitol-bis(poly-D,L-lactide)). Claim 7 recites that at least one of the constituents added in the process of claim 1 is water soluble. Claim 7 alternatively recites that at least one of the constituents employed in

the method of claim 1 is one which reacts with water to form a water-soluble resultant product and one which brings about a change in pH. Claim 9 recites that such a compound is sodium hydrogen carbonate (e.g. sodium bicarbonate). Claims 10 and 11 recite that the composition has added to it an agent which imparts adhesive properties between the finished composite and hard tissues (e.g. methacrylic acid-2-hydroxyethyl ester). Claim 15 recites that the amount of bone regeneration material mixed with the initiator (BRM_i), and the amount mixed with the activator (BRM_{ii}), is present at a ratio range of 1:10 to 10:1 (i.e. (BRM_i): (BRM_{ii}) = 1:10 to 10:1). Claim 18 recites that the polymerization initiator is a solution which is admixed with the bone regeneration material in an amount ranging from 0.1-20 wt%. Claim 19 recites that said initiator comprises an organic peroxide (e.g. dibenzoyl peroxide). Claim 21 recites that the polymerization activator is a solution which is admixed with the bone regeneration material in an amount ranging from 0.1-20 wt%. Claim 22 recites that said activator comprises such compounds as N,N-bis(2-hydroxyethyl)-p-toluidine. Claim 23 recites that both the activator and initiator compounds are used in the form of solutions and that they are mixed with the bone regeneration material. Claim 24 recites limitations to the bone regeneration material (e.g. calcium phosphate). Claim 25, as discussed above, recites that the bone regeneration materials mixed with the initiator and the activator are the same. Claim 26 recites that said materials are different. Claim 28 is broadly and reasonably interpreted as reciting that the method of claim 1 uses an interconnectingly porous bone regeneration material, thereby reciting the same subject matter as the base claim. Claim 29 recites that the bone regeneration material is crystalline, partially crystalline, glassy or amorphous. This is broadly and reasonably interpreted by the Examiner as reciting that said bone regeneration material may be in a form on any level of

ordered structure. Claim 30, as discussed above, is broadly and reasonably interpreted by the Examiner as reciting the same subject matter as claims 1 and 2. Claim 31 recites that the monomer or monomer mixture of claim 1 comprises terminal methacrylate groups.

Schnabelrauch et al. teach the preparation of the instant invention in Examples 4-6 of the DE '403 patent.

Initiator	25 Parts
	94.67 wt% calcium carbonate
	5.33 wt% dibenzoyl peroxide
Activator	25 Parts
	96.0 wt% calcium carbonate
	4.0 wt% bis-N,N-(2-hydroxyethyl)-p-toluidine
Polymerizing/Thickening Agent	50 Parts
	56 wt% dianhydro-D-glucitol-bis-[(oligo-L-lactyl) methacrylate]
	12 wt% methyl methacrylate
	12 wt% methacrylic acid-2-hydroxyethyl ester
	20 wt% dianhydro-D-glucitol-bis-(oligo-D,L lactide)

The Examples teach the separate formulation of the initiator/bone regeneration material and the activator/bone regeneration material mixtures as well as their ultimate mixture with the methacrylate-terminated monomer mixture (claim 31) and viscosity enhancing agent of claim 6. Per the Examples, the bone regeneration material mixed with both the initiator and activator are the same. The incorporation of water-soluble methacrylic acid-2-hydroxyethyl ester expressly

teaches the limitations of claims 7, 10 and 11. Example 1 expressly teaches the alternative limitations of claims 7 and 9 wherein a sodium bicarbonate solution is employed in the formation of the dianhydro-D-glucitol-bis-[(oligo-L-lactyl) methacrylate] component of the composite. The amounts of bone regeneration material used in each of the initiator and activator mixtures are present in about a 1:1 ratio (e.g. 94.67:96). Dibenzoyl peroxide in the amount of 5.33 wt% reads on claims 18 and 19. The use of 4.0 wt% bis-N,N-(2-hydroxyethyl)-p-toluidine reads on claims 21 and 22. Preparation of "Component B" (e.g. the initiator), per the DE '403 patent, is taught wherein the filler (e.g. bone regeneration material) is treated with a solution of the polymerization initiator with subsequent removal of the solvent (pg. 3 of the machine translation, lines 14-19). The preparation of the instant activator mixture is similarly taught in terms of "Component C" (pg. 3 of the machine translation, lines 22-27). Concerning the bone regeneration material limitations of claim 24, though the Examples are specifically and preferably drawn to formulations which employ calcium carbonate, the DE '403 also teaches the preferred use of such materials as calcium carbonate and hydroxyapatite (pg. 3 of the machine translation, lines 10-13). The same passage is further interpreted by the Examiner as teaching the limitations of claim 26 (objected to above), wherein mixtures of the preferred bone regenerating materials are used for forming Components "B" and "C". Thus the reference teaches each and every one of the instantly claimed limitations.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schnabelrauch et al. with respect to claim 1 as set forth above.

The limitations of claim 1 are discussed above. Claims 17 and 20 respectively recite, with regard to the preparation of the initiator mixture and the activator mixture that once said mixtures are formed, they are dried and then mixed with the liquid component of step (iii). The machine-translated text of the DE '403 patent does not expressly teach that each of the components are dried prior to mixture with one another. However, the methods for forming both

Components "B" and "C" (e.g. initiator and activator mixtures, respectively) do teach that the filler (e.g. bone regeneration material) in each component is mixed with an initiator solution (e.g. for "B") and an activator solution (e.g. for "C") and then subjected to the removal of the excess solvents. When considered in terms of Examples 4-6 wherein the filler material consists of 94.67% or greater of the component, it stands to reason that the removal of the excess liquid from the preparations would result in a relatively dry product.

It thus follows that the ordinarily skilled artisan would have had a reasonably high expectation of arriving at and achieving the instantly claimed method given the teachings that a small amount of initiator and/or activator solutions are initially admixed with the filler compound and then the excess liquid solvent removed. Such a teaching would have motivated the skilled artisan towards producing a dried product as a result of employing said method. Thus, in light of the forgoing interpretation and guidance of the prior art, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to have prepared a self-hardening bioabsorbable composite material such that a dried activator composition and dried initiator composition are admixed per the instant claims.

Claims 12-14, 16, 24, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schnabelrauch et al. with respect to claim 1 as set forth above, further in combination with Draenert et al. (USPN 4,373,217).

The limitations of claim 1 are discussed above. Claim 12 recites that at least one of the constituents employed in the method of claim 1 is a colorant or contrasting agent. Claims 13 and 14 recite that at least one of the constituents employed in the method of claim 1 is a

pharmaceutically active ingredient such as an antibiotic or anti-inflammatory agent. Claim 16 recites that the bone regeneration material used in the method is in the form of a powder or granules. The limitations of claim 24 are discussed above and are further noted as reciting more specific bone regeneration materials such as tricalcium phosphate. Claim 27 recites that the bone regeneration material employed in the method, such as calcium phosphate, are particles which have the following characteristics: pore diameters which range in size from 0.1-500 microns, particle sizes which range in size from 1-500 microns and a "BET" surface area of at least $0.1 m^2/g$. The limitations of claim 28 are discussed above, and are noted as further reciting more specific limitations for the bone regeneration material wherein it is calcium phosphate particles having a pore volume ranging from 0.4-3.3 mL/g (e.g. 400-3,300 μL/g).

The teachings to Schnabelrauch are discussed above. Of particular note is that calcium phosphate is expressly taught as a preferred filler or bone regeneration component. However, none of the property limitations recited in claims 16, 27 or 28 are expressly taught. Similarly, none of calcium phosphate species recited in claim 24 are taught. Also Schnabelrauch does not teach the incorporation of colorants or active ingredients into the composite prepared. However, the forgoing deficiencies are remedied by the teachings of Draenert et al.

The invention practiced by Draenert is drawn to tricalcium phosphate-based implantation materials (Abstract) which may be ultimately utilized as bone replacement or bone bonding/prosthesis material (col. 1, lines 6-10). Concerning the limitations of claim 24, Draenert teaches the use of more specific forms of porous calcium phosphate (e.g. tricalcium phosphate) (e.g. Examples 1 and 3a). Concerning the limitations of claim 12, Example 1 again expressly teaches the inclusion of chlorophyll in the bone cement mixture. Such a teaching is necessarily

interpreted as reading on the limitations of the claim given that an inherent property of chlorophyll is that it is a pigment which is found in most plants, algae and cyanobacteria, as is well known in the art (e.g. http://en.wikipedia.org/wiki/Chlorophyll). The ordinarily skilled artisan, in light of MPEP 2112.01, would highly expect the same pigmentation property to be conveyed in the teachings of Draenert, given that chemical compounds and their properties are not mutually exclusive. Concerning the limitations of claims 13 and 14, Draenert teaches the inclusion of antibiotic compounds (e.g. "-mycin" compounds) for the express purpose of avoiding or minimizing infections at the site of implantation (col. 6, line 30 to col. 7, line 17). Additional motivation for including such compounds stems from the teaching and suggestion that infections cannot always be prevented even when careful aseptic manipulation of the materials is observed (col. 6, lines 31-34).

Lastly, concerning the particle characteristics of the bone regeneration material, Example 1 teaches the limitations of claim 16 such that the tricalcium phosphate employed is a precipitated (e.g. solid form). As such it is expressly taught, if not suggested, that form used is particular. The average particle size of said tricalcium phosphate is further taught as ranging from 100-200 microns in diameter and having a pore volume of 0.4 mL/g.

Draenert does not expressly teach either the instantly claimed pore diameter or the instantly claimed "BET surface area" range. However, given that the teachings are directed to porous particles whose average diameter ranges from 100-200 microns, it stands to reason that the pores which enable the particles to have a "pore volume" must be less that 100-200 microns in size. It similarly follows that pore diameters of that range overlap and thus render obvious the instantly recited range. With regard to the "BET surface area" limitation recited in claim 27;

until some material difference(s) in the properties of the composition are demonstrated, said limitation is considered by the Examiner to be directed toward particles used in forming the composite of the instantly claimed method. It is further understood that "BET" refers to a theoretical method developed in 1938 by physicists ***B***runauer, ***E***mmett and ***T***eller wherein the physical adsorption of gas molecules on a solid surface served as the basis for an analytical technique for the measuring of the specific surface area of a material [***emphases added***] (http://en.wikipedia.org/wiki/BET_theory). It is respectfully pointed out that the Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether Applicants' method for using tricalcium phosphate particles comprising said property differs from and, if so, to what extent, from that which is taught and suggested by the reference(s). Therefore, with the showing of the reference, the burden of showing a lack of novelty and/or establishing non-obviousness by objective evidence is shifted to the Applicants (MPEP 2113).

Thus, based on the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonably high expectation of successfully arriving at the instantly claimed method. The ordinarily skilled artisan would have been particularly motivated by the combined guidance given the aforementioned advantages for including a pharmaceutically active ingredient and teachings of particle properties. Additional motivation to combine the references is garnered from the comparison of methods for producing the respective bone cements. Both references appear to preferably employ calcium phosphate, dimethyl-p-toluidine, and dibenzoyl peroxide as well as methyl esters of acrylic acid and methacrylic acid for forming the bioabsorbable bone composites.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, alone or in combination, especially in the absence of evidence to the contrary.

All claims have been rejected; no claims are allowed.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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